REMARKS

I. Support for the Amendments to the Claims

Claims 1-15, 17-18, 20-35 and 66 are currently in the application. Claim 18 has been amended.

Claim 18 has been amended to be dependent on claim 17, rather than claim 1, merely to provide the appropriate antecedent basis for the term "sodium dodecyl sulfate." Support for the amended claim 18 can be found throughout the specification and claims as originally filed, especially in the original language of claims 1, 17, and 18. No new matter has been added by the amendments to the claims.

Additional support for the amendment to claim 18 can be found in the language of original claims 1, 17, and 18 and in the specification, e.g., on page 13, lines 1-4; on page 16, lines 12-23; from page 18, line 5, to page 21, line 2; and in the Examples.

II. Status of the Claims

Claims 1-15, 17-18, 20-35 and 66 are currently in the application. Claim 18 has been amended.

III. The Telephonic Interview

Applicants thank the Examiners for their assistance with respect to the scheduling of the telephonic interview on January 14, 2010, and the discussion therein.

IV. The Rejection of Claims 1-15, 17-18, 20-35, and 66 Under 35 U.S.C. §112, First Paragraph, for Alleged Failure to Comply with the Written Description Requirement is Traversed

The Examiner has rejected claims 1-15, 17-18, 20-35, and 66 under 35 U.S.C. §112, first paragraph, for alleged failure to comply with the written description requirement. Applicants respectfully traverse this rejection for the reasons already discussed in the Supplemental Amendment and Response to Advisory Action, mailed October 2, 2008, and entered by the Examiner as noted in the Office Action, mailed February 6, 2009; for the reasons discussed during the Telephonic Interview of January 14, 2010; and for the following reasons.

In the Office Action, mailed August 25, 2009, the Patent Office now alleges:

> ....The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed. The phrases "subsequently contacting intact cells," "subsequently drying" and "a single solution" as amended in the response filed **5/30/09** have no support in the specification. Thus it constitutes new matter. [Par. 3, p. 2; all emphasis added.]

Applicants respectfully disagree.

To begin, this issue has already been raised by the Examiner (Advisory Action, mailed July 11, 2008) and addressed by the Applicants (Supplemental Amendment and Response to Advisory Action, mailed October 2, 2008). It was not reiterated by the Examiner in the Office Action that followed (mailed February 6, 2009).

To summarize the history of this rejection, the amendments described in the present Office Action were made in the Amendment filed on May 30, 2008. As noted in the Amendment:

> Support for the amendments to claims 1, 35, and 66 can be found throughout the specification and claims as originally filed. No new matter has been added by the amendments to the claims.
>
> Additional support for the amendments to claims 1, 35, and 66 can be found in the language of original claims 1, 35, and 66, respectively, and in the specification, e.g., from page 16, line 1, to page 18, line 3; from page 28, line 33, to page 30, line 8; and in the Examples. [Amendment, mailed May 30, 2008, p. 8.]

In the Advisory Action, mailed July 11, 2008, the Examiner refused to enter the Amendment, stating:

> The request for reconsideration has been considered but does NOT place the application in condition for allowance because: The newly added language raises new issues that would require further consideration and/or search. **The newly added languages "subsequently contacting intact cells", "subsequently drying" in claims 1, and 35 and "single solution" in claim 35 raise the issue of new matter.** Without entering the newly added languages, the rejections set forth in the Office action mailed 12/17/07 are maintained. [Pp. 1-2; all emphasis added.]

Applicants then filed a Request for Continued Examination (RCE) and the Supplemental Amendment and Response to Advisory Action, mailed October 2, 2008, noted above. In the Supplemental Amendment, Applicants provided citations throughout the specification to show that this language is amply supported by the specification and the claims as originally filed.

The Office Action of December 24, 2008, did not state that the Amendment of May 30, 2008, and the Supplemental Amendment of October 2, 2008, had been entered, so at Applicants request, the Examiner issued a new Office Action, mailed February 6, 2009.

Applicants respectfully note that the Examiner made no further mention of this rejection in the Office Action, mailed February 6, 2009.

Applicants also respectfully note that the claim amendments in the Amendment, mailed May 15, 2009, do not involve the phrases "subsequently contacting intact cells," "subsequently drying" and "a single solution" and that this issue has already been raised by the Examiner (Advisory Action, mailed July 11, 2008) and addressed by the Applicants (Supplemental Amendment and Response to Advisory Action, mailed October 2, 2008).

Despite the foregoing, the issue was raised again in the present Office Action, mailed August 25, 2009. Applicants addressed this issue at length during the Telephonic Interview on January 14, 2010.

As noted in the Supplemental Amendment and Response to Advisory Action, mailed October 2, 2008, and for the reasons discussed during the Telephonic Interview of January 14, 2010, as well as for the sake of completeness, Applicants provide the following remarks.

A. "Subsequently"

With respect to the use of "subsequently contacting intact cells" and "subsequently drying," Applicants submit that this language is amply supported by the specification and the claims as originally filed.

First, claims 1, 35, and 66 are method claims reciting a series of steps, which would imply to one of ordinary skilled in the art, who is familiar with laboratory protocols, that the steps are sequential, similar to a lab protocol or recipe. Although the word "comprising" is used, the amendments to the claims with the term "subsequently" provide order to the steps.

In particular, the specification states:

> The present method provides a quick, simplified, cost effective method for storing, and ***subsequently*** isolating, nucleic acids using a wide range of commercially available solid phase media, which until now have been considered inappropriate for storage....[P. 11, ll. 9-12; emphasis added.]

Second, the language of the Examples with respect to the protocol clearly indicates the sequential order of the method steps of claims 1 and 35. The Examiner's attention is directed to the initial paragraph, particularly to the following:

> ....25-50 µl FTA® solution (Whatman) were applied to each column ***after*** Nucleated Cell Capture and Red Cell Lysis Step. ***Then*** columns were left at room temperature for drying, storage and subsequent DNA extraction. [P. 32, ll. 5-7; all emphasis added.]

The Examiner's attention is also directed to the "Study design for Examples 1-4" (p. 32, ll. 14-32), the "Study design" for Example 5 (p. 35, ll. 18-29), the "Study design" for Example 6 (p. 37, ll. 6-18), the "Study design" for Example 7 (p. 37, l. 34, to p. 38, l. 17), the "Study design" for Example 8 (p. 39, ll. 8-20), and the "Study design" for Example 9 (p. 40, ll. 1-17) with respect to filters/media of various types. One of ordinary skill in the art would understand that the steps in these laboratory protocols were intended to be performed in their stated order.

In the "Study design for Examples 1-4" (p. 32, ll. 14-32), the laboratory protocol has the following ordered steps: (i) application of human whole blood onto the column; (ii) washing of the column with a red-cell lysis buffer; (iii) application of lysis solution to the column; (iv) drying of the column; (v) storage of the column; (vi) isolation of DNA from the column; and (vii) evaluation of the DNA quality and quantity.

In the "Study design" for Example 5 (p. 35, ll. 18-29), the laboratory protocol has the following ordered steps: (i) application of blood onto the column; (ii) washing of the column

with a washing solution; (iii) application of lysis solution to the column (with no application of lysis solution to the control); (iv) storage of the column at ambient conditions; (v) isolation of DNA from the column; and (vi) evaluation of the DNA quality and quantity.

In the "Study design" for Example 6 (p. 37, ll. 6-18), the laboratory protocol has the following ordered steps: (i) application of whole blood onto the column; (ii) washing of the column with a washing solution; (iii) application of lysis solution to the column (with no application of lysis solution to the control group); (iv) drying and storing of the column; (v) isolation of DNA from the column; and (vi) evaluation of the DNA quality and quantity.

In the "Study design" for Example 7 (p. 37, l. 34, to p. 38, l. 17), the laboratory protocol has the following ordered steps: (i) application of whole blood onto the column; (ii) washing of the column with a washing solution; (iii) application of lysis solution to the column (with no application of lysis solution to the control group); (iv) drying and storing of the column; (v) isolation of DNA from the column; and (vi) evaluation of the DNA quality and quantity.

In the "Study design" for Example 8 (p. 39, ll. 8-20), the laboratory protocol has the following ordered steps: (i) application of whole blood onto the column; (ii) washing of the column with a washing solution; (iii) application of lysis solution to the column (with no application of lysis solution to the control group); (iv) drying and storing of the column; (v) isolation of DNA from the column; and (vi) evaluation of the DNA quality and quantity.

In the "Study design" for Example 9 (p. 40, ll. 1-17), the laboratory protocol has the following ordered steps: (i) application of white blood cells onto the column; (ii) washing of the column with a washing solution; (iii) application of lysis solution to the column (with no application of lysis solution to the control group); (iv) drying and storing of the column; (v) isolation of DNA from the column; and (vi) evaluation of the DNA quality and quantity.

In each instance, the Study Design fully describes the ordered steps of claims 1, 35, and 66 in the order described in those claims. Similar support can be found in the Abstract as originally filed in PCT/US2003/031483 (filed October 3, 2003), of which the present application is a national phase application.

Claims 2-15, 17-18, and 20-34 are dependent, either directly or indirectly, on claim 1 as an underlying claim, and the same reasoning would apply to these dependent claims.

Thus, the use of "subsequently" with respect to "subsequently contacting intact cells" and "subsequently drying" the medium does not add new matter.

B. "Single Solution"

With respect to the use of "single solution," Applicants submit that this language is likewise amply supported by the specification and the claims as originally filed.

First, the "single solution" is supported by the original language of the claims (e.g., original claims 35, and 66), which recite:

> ...a solution comprising:
> i. a weak base;
> ii. a chelating agent; and
> iii. an anionic surfactant or detergent. [***original*** claims 35 and 66]

The "solution" clearly combines all three of these elements (although it is not restricted to them). (The Examiner's attention is also directed to original claim 19 [with underlying claim 1]. Claim 19 has since been canceled, and claim 1 has since been amended to include limitations from claim 19.)

Second, the language of the specification clearly indicates that the solution of claim 35 is one, single solution. The Examiner's attention is directed to the Detailed Description (e.g., from p. 18, l. 5, to p. 20, l. 2), which describes not merely the various types of bases, chelating agents, and anionic surfactants/detergents that can be used, but their combination into a single solution.

For example:

> The chemical composition of ***the solution***, which...more preferably comprises a weak base, a chelating agent, and an anionic surfactant or detergent, facilitates the lysis of whole cells and the subsequent capture of the released nucleic acids. ***The*** chemical ***composition*** further aids in their long term storage....[P. 18, ll. 5-9; all emphasis added.]

And also:

> ....***The*** chemical ***solution*** can include a weak base, a chelating agent, and the anionic surfactant or detergent, and optionally uric acid and urate salt as discussed in detail in the above-cited United States Patent 5,807,527.... [P. 18, ll. 26-29; all emphasis added.]

And also:

> In one preferred embodiment, ***the solution*** used in this aspect of this invention comprises the following:
>
> (i) a monovalent weak base (such as "Tris", tris-hydroxymethyl methane, either as the free base or as the carbonate);
>
> (ii) a chelating agent (such as EDTA, ethylene diamine tetracetic acid); and
>
> (iii) an anionic detergent (such as SDS, sodium dodecyl sulfate); and optionally
>
> (iv) uric acid or a urate salt.

> An example of one preferred embodiment of ***the solution*** is an FTA® solution (Whatman, Inc.) comprising Tris, EDTA, SDS, and uric acid. [P. 19, ll. 1-9; all emphasis added.]

Grammatically, the specification refers to "the solution" and "the chemical composition" in the singular, which supports the "single solution" terminology of the claims.

In addition, the FTA® solution is also described as an "FTA® cocktail" (p. 20, l. 27), and the disclosure of the aforementioned U.S. Patent 5,807,527 is incorporated by reference, in addition to U.S. Patents 5,756,126 and 5,496,562 (see, e.g., p. 18, l. 20 and from p. 40, l. 33, to p. 41, l. 3). These three patents each describe a solution comprising a weak base, a chelating agent, and an anionic surfactant or detergent.

Moreover, the Examiner's attention is directed to the Examples and directed to the initial paragraph, particularly to the following:

> ....25-50 µl ***FTA® solution (Whatman)*** were applied to each column after Nucleated Cell Capture and Red Cell Lysis Step.... [P. 32, ll. 5-6; all emphasis added.]

The Examiner's attention is also directed to the "Study design for Examples 1-4" (p. 32, ll. 19-21), the "Study design" for Example 5 (p. 35, ll. 22-24), the "Study design" for Example 6 (p. 37, ll. 10-12), the "Study design" for Example 7 (p. 38, ll. 7-11), the "Study design" for Example 8 (p. 39, ll. 12-14), and the "Study design" for Example 9 (p. 40, ll. 8-10) with respect to the use (or absence) of an aliquot of FTA® solution or FTA®-like solution (without uric acid).

In the "Study design for Examples 1-4" (p. 32, ll. 19-21), the laboratory protocol describes a single solution comprising a weak base (Tris), a chelating agent (EDTA), and an

anionic surfactant/detergent (SDS). The same single solution is described in the laboratory protocol of the "Study design" for Example 5 (p. 35, ll. 22-24), the "Study design" for Example 6 (p. 37, ll. 10-12), the "Study design" for Example 8 (p. 39, ll. 12-14), and the "Study design" for Example 9 (p. 40, ll. 8-10).

Other examples of a single solution, each having a weak base (Tris), a chelating agent (EDTA), and an anionic surfactant/detergent (SDS), are described in the "Study design" for Example 7 (p. 38, ll. 7-11) and the "Study design" for Example 9 (p. 40, ll. 8-10).

Clearly, the above passages describe a single aliquot of solution comprising various elements – not a series of sequentially added solutions.

Thus, the use of "single solution" does not add new matter or raise any new issue that would require further consideration or searching.

Applicants respectfully submit that claims 1-15, 17-18, 20-35, and 66 fulfill the requirements of 35 U.S.C. §112, first paragraph, thereby placing these claims in condition for allowance, and request the Examiner's reconsideration accordingly.

V. The Rejection of Claims 1-11, 14-15, 17, 20, 26, 28-30, 32-35, and 66 under 35 U.S.C. §103(a) over Smith is Traversed

The Examiner has rejected claims 1-11, 14-15, 17, 20, 26, 28-30, 32-35, and 66 under 35 U.S.C. 103(a) as unpatentable over Smith et al. (U.S. Patent 6,645,717; issued November 11, 2003; "Smith"). Applicants traverse the rejection and respectfully request reconsideration of these claims.

The Patent Office alleges, in pertinent part:

> Smith et al. disclose a medium for storage of a genetic material and a method for storing the genetic material. The medium includes a support for immobilizing a genetic material and a coating associated with the support for enabling cellular lysis and releasing the genetic material from the lysed cells (see column 4, lines 10-17). The method includes the steps of immobilizing the genetic material on the support and while enabling cellular lysis and releasing the genetic material from the lysed cells. The genetic material is eluted (see column 4, lines 18-25). The blood is spotted to the filter membrane of the invention, air dried for two minutes and stored at room temperature for 19 weeks (see column 17, lines 66-67 and column 18, lines 1-6). The medium is a plurality of fibers with disordered structure (see column 5, lines 45-46 and fig. 9). The filter media is cellulose-based (see column 6, lines 35-37). The chemical coating solution includes a week base, chelating agent, an anionic surfactant or detergent which can between 65°C and 100°C for elution (see column 8, lines 51-58). In one of the examples the filter membrane is washed several times before elution (see column 15, lines 47-59). [Par. 5, pp. 3-4; all emphasis added.]

Applicants respectfully disagree and traverse this rejection for the reasons discussed during the Telephonic Interview on January 14, 2010, and for the following reasons.

Essentially, the Patent Office alleges that Smith discloses drying DNA samples on a card and storing them, but it should be noted that Smith fails to disclose adding a solution to an already applied sample. Instead, the coating of Smith is added to the matrix and dried prior to the application of the sample, and the combination of support and chemical coating produces the filter membrane of the invention prior to application of the sample:

> *The present invention*, generally shown at **10** in FIG. 9, *includes* the following components:
> (i) *a suitable support*, preferably a filter membrane **12**; *and*
> (ii) *a chemical coating* **14**.
>
> *Reaction of the filter membrane with the chemical coating solution produces the filter membrane of the invention*....[Col. 6, ll. 23-29; bold in original; all other emphasis added.]

And also:

> ....The composition of the chemical coating solution is as described and relates to that outlined in U.S. Pat. Nos. 5,756,126, 5,807,527, and 5,496,562. ***Adsorption of the chemical coating solution to the selected filter membrane results in the formation of the filter membrane of the invention.*** [Col. 6, ll. 59-61; all emphasis added.]

The coating is applied prior to the application of the sample:

> The filter membrane of the invention can possess the same chemical component as FTA that enables the action of cellular lysis and nucleic acid release ***upon sample application***. [Col. 7, l. 66, to col. 8, l. 2; all emphasis added.]

This sequence is clearly demonstrated in the protocols described in the Examples. In Example 1, several drops of blood were "spotted to the filter membrane of the invention" (col. 11, ll. 4-6), the "filter membrane of the invention" having already been defined as a combination of a support and a chemical coating (col. 6, lines 23-29 and 59-61, and from col. 7, line 66, to col. 8, line 2). Example 2 (col. 11, lines 52-54), Example 3 (col. 12, lines 50-54), Example 4 (col. 13, lines 42-45), Example 5 (col. 14, lines 30-31), Example 7 (col. 16, lines 65-67), and Example 8 (col. 17, lines 54-57; from col. 17, line 66, to col. 18, line 1) also describe the spotting of blood or saliva on the filter membrane of the invention (i.e., spotting of the sample onto the previously coated support).

While it is true that Smith describes a composition comprising a weak base, a chelating agent, an anionic surfactant or anionic detergent, and optionally uric acid or a urate salt, and while Smith also describes drying the filter, it should be noted that Smith fails to mention adding the solution of the present invention to the already applied sample. Instead, the solution of Smith is added to the support and dried prior to the application of the sample.

In essence, a key difference between Smith and the present invention is that in Smith, the chemical composition is deposited on the support and dried and then is contacted by a cellular sample, whereas in the present invention, the solution is applied to the solid matrix after the matrix contains the sample.

Applicants also wish to point out the advantages of the present invention. As a practical matter, the filter of Smith can only contain a finite amount of the coating solution, because only so much solution can adsorb to the support, which also limits the number of cells that can be lysed by the finite amount of solution. In contrast, using the present invention, the cells can be concentrated in the medium prior to application of indefinite amounts of solution (see, e.g., claims 35 and 66).

In addition, all the cell types in a mixed cell sample placed on the filter of Smith would be expected to be lysed upon contacting the filter, whereas in the method of the present invention, cells of a desired cell type can be isolated on the solid phase medium and the other cells removed prior to application of the solution and lysis of the entrapped cells of only the desired cell type.

Nothing in Smith would suggest to one of skill in the art that it would produce the present invention (solution application following sample application and subsequent drying). In contrast, in the present invention, ***the sample is added to the solid phase medium first and then the solution*** (comprising (i) an anionic surfactant or detergent, (ii) a weak base, and (iii) a chelating agent; step d), ***followed by drying and storage***. Therefore, the present invention is distinguishable from Smith.

Thus, there is no teaching, suggestion, or motivation in Smith that would have led one of ordinary skill in the art to modify these teachings to arrive predictably at the claimed invention, nor is the present invention merely a variation on known work in the field of endeavor that would have been predictable to one of ordinary skill in the art, nor is it chosen from a finite number of identified, predictable solutions, with a reasonable expectation of success. In the present invention, therefore the improvement is more that the predicable use of prior art elements according to their established functions. (Examination Guidelines for

Determining Obviousness under 35 U.S.C. 103 in View of the Supreme Court Decision in *KSR International Co. v. Teleflex Inc.*, Fed. Reg. 72(195): 57526-57535 [Oct. 10, 2007]).

Claims 2-11, 14-15, 17, 20, 26, 28-30, and 32-34 are dependent, either directly or indirectly, on claim 1 as an underlying claim and the same reasoning applies to these dependent claims.

Applicants respectfully submit that remaining claims 1-11, 14-15, 17, 20, 26, 28-30, 32-35, and 66 fulfill the requirements of 35 U.S.C. §103(a), thereby placing these claims in condition for allowance, and request the Examiner's reconsideration accordingly.

VI. The Rejection of Claims 12, 21-25, 27, and 31 under 35 U.S.C. §103(a) over Smith in view of Mitchell is Traversed

The Examiner has rejected claims 12, 21-25, 27, and 31 under 35 U.S.C. 103(a) as unpatentable over Smith et al. (U.S. Patent 6,645,717; issued November 11, 2003; "Smith") in view of Mitchell et al. (WO 00/21973; issued April 20, 2000; "Mitchell"). Applicants traverse the rejection and respectfully request reconsideration of these claims.

Claims 12, 21-25, 27, and 31 are dependent, either directly or indirectly, on underlying claim 1, which was rejected for alleged obviousness over Smith. Therefore, the above arguments with respect to claim 1 and the rejection over Smith also apply to the rejection of claims 12, 21-25, 27, and 31 over Smith in view of Mitchell.

After acknowledging that "Smith et al. do not disclose the limitations of claims 12, 21-25, 27 and 31" (par. 6, p. 6), the Patent Office alleges, in pertinent part:

> One of ordinary skill in the art would have been motivated to apply a fiber diameters selected from the range of 1 um to 10 um and the techniques of Mitchell et al. for condensing material from a cellular nucleus, rupturing intact whole cells retained by a solid phase medium to leave condensed material on the medium, lysing the condensed material, retaining nucleic acid on the medium by non-ionic interaction and physical retarding movement of nucleic acid through a solid phase medium because these techniques were well known in the art and by doing so the method substantially improves the yield and purity of nucleic acid products (see pg. 6, last paragraph). It would have been prima facie obvious to apply these techniques as claimed for isolating and storing nucleic acid. [Par. 6, pp. 6-7; underline in original.]

Applicants respectfully disagree and traverse the rejection – with respect to Smith for the reasons as applied to underlying claim 1, as discussed above, and with respect to Mitchell for reasons already discussed at length throughout prosecution of the present application, particularly in the Amendment mailed May 30, 2008, and in the Amendment mailed May 15, 2009, as well as during the Telephonic Interview on January 14, 2010.

As discussed above, while it is true that Smith discloses drying the filter, it should be noted that Smith fails to mention added a solution to the already applied sample. Instead, the solution of Smith is added to the filter and dried prior to application of the sample.

Applicants respectfully submit that Mitchell fails to supply the deficiencies of Smith.

In the present language of claim 1, the sample is added to the solid phase medium first and then the solution (comprising a weak base, a chelating agent, and an anionic surfactant or detergent). Therefore, the ***present invention*** is distinguishable in that ***one solution*** is added to the sample and ***not multiple solutions added sequentially as in Mitchell***.

Similarly, in Smith, one solution is applied as a chemical coating to the support to form the filter.

Another distinction is the drying of the sample for storage and archiving of DNA. Mitchell states (p. 7, ll. 15-20) that if the filter is allowed to dry, the DNA is recoverable but sheared and, where the method is carried out in a column, indicates the need for using a vapor block to prevent drying from occurring, because this is undesirable. ***Such a method is in contrast to the present invention, in which the medium is dried without shearing (unlike Mitchell, in which drying is equated with shearing).***

Therefore, Mitchell teaches away from both the present invention and Smith. One of ordinary skill in the art would not have been motivated to combine Mitchell with Smith, and such a combination would not have been expected to produce the present invention. If Mitchell had read Smith, he would surely have assumed that it was impossible to dry out his column ***unless*** he had ***pre*-protected** his column material to prevent it from degrading the DNA. It is the present invention which – ***surprisingly*** – showed that one did not need to protect the column beforehand, but that one could include the necessary protecting and lysing agents all in one solution and ***subsequently*** apply this to the already trapped nucleic acid-containing cells. It is ***surely quite surprising*** that enough of the protecting agents will stick on the column to prevent degradation and allow one to dry out the material for elution at a later stage. It is also very practical, because one can defer the point at which one needs to isolate and test the DNA itself.

Furthermore, although the specification mentions TRITON as a detergent, the present language of claim 1 reflects a preferred embodiment in which the solution comprises an anionic detergent or surfactant (such as SDS), as well as a weak base and a chelating agent (see, e.g., p. 19, lines 1-9; and from p. 20, line 3, to p. 21, line 2).

Moreover, in Mitchell, the SDS and TE are not part of the same solution, but the current claim 1 is directed to "a solution comprising (i) an anionic surfactant or detergent, (ii) a weak base, and (iii) a chelating agent." In Mitchell, the SDS and TE are added separately and filtered to waste.

Mitchell uses a lysis buffer (such as a detergent) to lyse the cells, but then follows this step with a low salt buffer (e.g., TE^{-1} or water) (see pp. 7-8, 14-15; see also Example 1 [p. 18: lysis by 0.5% SDS, followed by washing with TE]). The effect of this second wash, however, is to wash out any remaining anionic detergent, which as noted by Dr. Walter King during the Telephonic Interview on January 14, 2010, would remove the anions, leaving the isolated nucleic acid unprotected after drying and subject to degradation, unlike the present invention in which at least some portion of the anionic surfactant/detergent-containing solution is dried on the medium.

In addition, the present claims are directed to a method wherein the cell lysate comprises nucleic acid. While the specification of the present application also describes an alternative method including a separate lysis step for nuclei using a "low-salt, non-isotonic buffer, such as a hypotonic buffer" (see, e.g., page 17, lines 1-29), the present claims are directed to the use of an anionic surfactant or detergent, which "increases the yield and purity of the DNA product" the use of which results in the nucleic acid being "retained by the media" (see, e.g., page 16, lines 7-29, and page 17, line 31).

Nothing in Mitchell would suggest to one of skill in the art that it should be combined with Smith, or *vice versa*, to produce the present invention (single solution application following sample application and subsequent drying for archiving). In particular, one of skill in the art would not cite Mitchell's method for archiving since Mitchell specifically teaches away from drying, as it harms the nucleic acid and reduces yield.

Specifically, in Mitchell, ***multiple lysis solutions*** are added ***sequentially*** in order to function, and Mitchell ***teaches away from drying***, as it **shears the nucleic acid** and **reduces yield**. Smith uses a chemical composition of the base, chelator, detergent and uric acid/urate salt ***that is already deposited*** on the solid matrix ***and dried prior to exposure*** to the cells.

In contrast, in the present language of underlying claim 1, ***the sample is added to the solid phase medium first and then the single-solution archiving agent*** (a solution comprising (i) an anionic surfactant or detergent, (ii) a weak base, and (iii) a chelating agent; step d), ***followed by drying and storage***. Therefore, the present invention is distinguishable from both Mitchell and Smith, either alone or in combination with one another.

Moreover, for the reasons discussed above, not only do the teachings of Mitchell fail to supply the deficiencies of Smith, the teachings of Mitchell and Smith are incompatible and the two references teach away from each other.

Thus, there is no teaching, suggestion or motivation in Smith or Mitchell that would have led on of ordinary skill in the art to combine and/or modify these teachings to arrive at the claimed invention, nor is the present invention merely a variation on known work in the field of endeavor that one of ordinary skill in the art would have been predictable to one of ordinary skill in the art, nor is it chosen from a finite number of identified, predictable solutions, with a reasonable expectation of success. In the present invention, therefore, the improvement is more than the predictable use of prior art elements according to their established functions. (Examination Guidelines for Determining Obviousness under 35 U.S.C. 103 in View of the Supreme Court Decision in *KSR International Co. v. Teleflex Inc.*, Fed. Reg. 72(195): 57526-57535 [Oct. 10, 2007]).

Applicants respectfully submit that claims 12, 21-25, 27, and 31 fulfill the requirements of 35 U.S.C. §103(a), thereby placing these claims in condition for allowance, and request the Examiner's reconsideration accordingly.

VII. The Rejection of Claim 13 and 18 under 35 U.S.C. §103(a) over Smith in view of Mullis is Traversed

The Examiner has rejected claims 13 and 18 under 35 U.S.C. 103(a) as unpatentable over Smith et al. (U.S. Patent 6,645,717; issued November 11, 2003; "Smith") in view of Mullis (U.S. Patent 5,187,083; issued February 16, 1993; "Mullis"). Applicants traverse the rejection and respectfully request reconsideration of these claims.

Claims 13 and 18 are indirectly dependent on underlying claim 1, which was rejected for alleged obviousness over Smith. Therefore, the above arguments with respect to claim 1 and the rejection over Smith also apply to the rejection of claims 12, 21-25, 27, and 31 over Smith in view of Mullis.

The Patent Office alleges, in pertinent part:

> One of ordinary skill in the art would have been motivated to apply the filter of Mullis with the pore size which is from about 0.2 microns to about 0.8 microns and the lysis buffer containing 1% of SDS because the filter and the lysis buffer of Mullis are used in obtaining substantially purified DNA from a biological sample (See column 3, lines 21-22). It would have been prima facie obvious to apply the filter of Mullis with the pore size which is from about 0.2 microns to about 0.8 microns and the lysis buffer containing 1% of SDS for isolating nucleic acid as claimed. [Par. 7, p. 8; underline in original.]

Applicants respectfully disagree and traverse the rejection – with respect to Smith for the reasons as applied to underlying claim 1, as discussed above, and with respect to Mullis for reasons already discussed at length throughout prosecution of the present application, particularly in the Amendment mailed May 30, 2008, and in the Amendment mailed May 15, 2009.

As discussed above, while it is true that Smith discloses drying the filter, it should be noted that Smith fails to mention added a solution to the already applied sample. Instead, the solution of Smith is added to the filter and dried prior to application of the sample.

Applicants respectfully submit that Mullis fails to supply the deficiencies of Smith.

In addition, Mullis ***produces lysate first*** and ***then traps this on a filter*** followed apparently by ***elution without any suggestion of intermediate drying***. One of ordinary skill in the art would certainly not have turned to Mullis for any suggestion that one could dry before elution.

Thus, there is no teaching, suggestion or motivation in Smith or Mullis that would have led one of ordinary skill in the art to combine and/or modify these teachings to arrive at the claimed invention, nor is the present invention merely a variation on known work in the field of endeavor that one of ordinary skill in the art would have been predictable to one of ordinary skill in the art, nor is it chosen from a finite number of identified, predictable solutions, with a reasonable expectation of success. In the present invention, therefore, the improvement is more than the predictable use of prior art elements according to their established functions. (Examination Guidelines for Determining Obviousness under 35 U.S.C. 103 in View of the Supreme Court Decision in *KSR International Co. v. Teleflex Inc.*, Fed. Reg. 72(195): 57526-57535 [Oct. 10, 2007]).

Applicants respectfully submit that claims 13 and 18 fulfill the requirements of 35 U.S.C. §103(a), thereby placing these claims in condition for allowance, and request the Examiner's reconsideration accordingly.

VIII. Additional Remarks

In the Office Action, mailed February 6, 2009, the Examiner had expressly maintained an earlier rejection of claims 1-12, 14-35, and 66 under 35 U.S.C. §103(a) as allegedly unpatentable over Mitchell (WO 00/21973; issued April 20, 2000) in view of Burgoyne (U.S. Patent 5,496,562; issued March 5, 1996) and an earlier rejection of claim 13 under 35 U.S.C. 103(a) as allegedly unpatentable over Mitchell (WO 00/21973; issued April 20, 2000) in view

of Burgoyne (U.S. Patent 5,496,562; issued March 5, 1996) as applied to claims 1-12, 14-35, and 66 and further in view of Mullis (U.S. Patent 5,187,083; issued February 16, 1993).

Applicants addressed these rejections at length in the Amendment, mailed May 15, 2009. In the present Office Action (mailed August 25, 2009), the Examiner has not reiterated these rejections and has not addressed Applicants' remarks except to note that the arguments "are moot in view of the new ground(s) of rejection" (par. 1, p. 2). In addition, the Patent Office never raised these issues during the Telephonic Interview on January 14, 2010, even when these previous rejections were mentioned.

Therefore, Applicants respectfully request that the Examiner expressly confirm withdrawal of these rejections under 35 U.S.C. §103(a) over Mitchell and Burgoyne or over Mitchell, Burgoyne, and Mullis.

CONCLUSION

It is believed that all the claims are in condition for allowance. If discussion of any amendment or remark made herein would advance this important case to allowance, the Examiner is invited to call the undersigned as soon as convenient.

In view of the foregoing amendments and remarks, the present application is respectfully considered in condition for allowance. An early reconsideration and notice of allowance are earnestly solicited.

Applicants hereby request a two-month extension of time for the Amendment and accompanying materials. If, however, a petition for an additional extension of time is required, then the Examiner is requested to treat this as a conditional petition for an additional extension of time and the Commissioner is hereby authorized to charge our deposit account no. 04-1105 for the appropriate fee. Although it is not believed that any additional fee (in addition to the fee concurrently submitted) is required to consider this submission, the Commissioner is hereby authorized to charge our deposit account no. 04-1105 should any fee be deemed necessary.

Respectfully submitted,

Date: January 25, 2010

Kathryn A. Piffat, Ph.D., (Reg. No. 34,901)
EDWARDS ANGELL PALMER & DODGE, LLP
P.O. Box 55874
Boston, Massachusetts 02205
Telephone: 617-239-0100
Facsimile: 617-227-4420